REMARKS

Claims 1, 2, 4-15, 19 and 20 are pending in the instant application. Claims 1, 2, 4-15, 19 and 20 have been rejected. Claims 11, 19 and 20 have been canceled. Claim 1 has been amended. No new matter has been added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

I. Rejection of Claims Under 35 U.S.C. 103(a)

The rejection of claims 1, 2, 4-15, 19 and 20 under 35 U.S.C. 103(a) as being unpatentable over Honda et al. (1999), Loijens et al. (1996), and further in view of Weintraub (1990), Baracchini et al. (US Patent 5,801,154), and Fritz et al. (1997) has been maintained. The Examiner suggests it would have been *prima facie* obvious for one of ordinary skill to be motivated to make antisense oligonucleotides as claimed because the cited art teaches a physiological role for the protein in membrane ruffle formation and regulation of signal transduction, while Loijens et al. teach the variants claimed as being derived from phosphatidylinositol-4-phosphate 5-kinase, Iα, including SEQ ID NO: 3. The Examiner suggests it would have been obvious then to make antisense

oligonucleotides encoding phosphatidylinositol-4-phosphate 5-kinase, Iα since Weintraub teach antisense nucleic acids can selectively inhibit the activity of genes and gene expression. The Examiner then suggests that one of skill would have a reasonable expectation of success in modifying antisense compounds as claimed based on the teachings of Baracchini and Fritz. Applicants respectfully traverse this rejection.

At the outset, Applicants again state that they disagree with the Examiner's conclusions regarding the teachings as combined because none of the cited art teach antisense compounds specifically targeted to phosphatidylinositol-4-phosphate 5-kinase, Iα. It is only with the specification in hand that one of skill would understand how to make and use antisense as claimed. However, in an earnest effort to advance the prosecution of this case, Applicants have canceled claims 11, 19 and 20 and amended the remaining claims to recite that the antisense compounds are targeted to specific nucleobase regions within specific target regions of the sequence of phosphatidylinositol-4-phosphate 5-kinase, Iα (SEQ ID NO: 3). Support for these amendments can be found throughout the specification as filed but in particular at Tables 1 and 2.

Honda et al. (1999) disclose only the biological role of phosphatidylinositol-4-phosphate 5-kinase, Iα as a downstream effector of small G protein ARF6 in membrane ruffle formation. Nowhere does this reference teach or suggest use of antisense compounds of any type to target the phosphatidylinositol-4-phosphate 5-kinase, Iα gene and to inhibit its expression using antisense. As a result, this reference also fails to teach or suggest antisense compounds as now claimed.

Loijens et al. (1996) disclose the peptide sequence of phosphatidylinositol-4-phosphate 5-kinase, Iα isolated from bovine erythrocytes and then the full-length cDNA coding phosphatidylinositol-4-phosphate 5-kinase, Iα and two predicted splice variants that were cloned from a human fetal brain cDNA library. The paper reports the distribution of phosphatidylinositol-4-phosphate 5-kinase, Iα in tissues. However, nowhere does this paper teach or suggest antisense compounds of any type targeted to any nucleobase region within a target region of phosphatidylinositol-4-phosphate 5-kinase, Iα of SEQ ID NO: 3 as claimed. It is only with the specification in hand that one of skill has evidence that targeting antisense to regions of

phosphatidylinositol-4-phosphate 5-kinase, Iα could successfully inhibit expression of this gene.

Therefore, none of the primary references, either alone or when combined, teach or even suggest use of antisense compounds of any type for inhibition of expression of phosphatidylinositol-4-phosphate 5-kinase, Iα, including antisense compounds as now claimed. The secondary references cited fail to overcome the deficiencies in teaching of these primary references.

Weintraub (1990) is an older paper on the technology of antisense and only discusses the use of antisense as a research tool. Nowhere does this paper teach or suggest antisense compounds of any type targeted to phosphatidylinositol-4-phosphate 5-kinase, Iα of SEQ ID NO: 3 as now claimed. Additionally, this paper explicitly states at page 46 that "many important refinements of antisense technology are still needed, and many important questions must still be answered..." Thus, one of skill in the art would not understand using this paper that antisense technology would be successfully used to inhibit expression of any gene, without evidence of such use.

The '154 patent teaches modification to antisense oligonucleotides in general as a way to enhance activity. However,

this general discussion of modified oligonucleotides does not teach or suggest use of antisense compounds of any type to target a specific gene, phosphatidylinositol-4-phosphate 5-kinase, Iα, or a specific region of this gene, and the successful inhibition of expression using antisense.

Fritz et al. (1997) is a paper that describes carrier systems for antisense oligonucleotides, in general terms. Nowhere does this paper teach or suggest antisense compounds of any type targeted to any region within the phosphatidylinositol-4-phosphate 5-kinase, Iα of SEQ ID NO: 3 as claimed.

To establish a *prima facie* case of obviousness, three basic criteria must be met. MPEP 2143. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations. Mere teaching of the function of a gene and/or its protein product and then teaching of antisense technology in general does not provide one of skill with the expectation of success in developing antisense targeted to a specific gene. The limitations of the

claims as filed, which specify antisense compounds targeted to phosphatidylinositol-4-phosphate 5-kinase, Iα of SEQ ID NO: 3, or variant thereof, are not taught or even suggested by any of the references individually or when combined. Further, the claims as now amended further specify nucleobase regions within the sequence of SEQ ID NO: 3 and are also not taught or suggested by any of these references when alone or when combined. Therefore, the limitations of the claims as amended clearly are not taught or suggested by the combination of prior art references, nor is any expectation of successful use of such antisense compounds provided by the combination of prior art. It is only with the specification in hand that one of skill would understand that antisense compounds targeted to phosphatidylinositol-4-phosphate 5-kinase, Iα could be used to inhibit expression of this gene. Thus, the combination of prior art cited cannot render the instant claimed invention obvious. Withdrawal of this rejection is therefore respectfully requested.

II. Rejection of Claims Under 35 U.S.C. 112, Second Paragraph

Claim 19 has been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point

out and distinctly claim the subject matter which applicant regards as the invention. The Examiner suggests that the claim recites "differentially inhibits" and this standard is not reasonably ascertained based on the disclosure of the specification as filed. Applicants have canceled claim 19, therefore, withdrawal of this rejection is respectfully requested.

III. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

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